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Editorial

Trigonella Foenum Graecum (Fenugreek) as a Potential Cancer Chemo-Preventive Agent

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Editorial

Cancer is among the greatest health challenges being faced by the human race today. Common treatments for various cancers, including surgery, radiation therapy, and chemotherapy, have very low success rates. Two of the most frequently used chemotherapeutic drugs, 5-fluorouracil (5-FU) and cisplatin, cause side effects such as bone marrow suppression, gastrointestinal toxicity and renal damage, the problems that are still to be resolved [1]. To overcome such side effects and limitations, the direction of present research for novel antitumor agents has shifted towards natural products, especially plants used in traditional medicine. Most natural products target multiple gene products and thus are ideally suited for prevention and treatment of cancer which has the involvement of many genes. Fenugreek (*Trigonella foenum graecum*) is an annual herb that belongs to the family Leguminosae and is currently one of the major natural products being explored for its potential anticancer properties. Many of the pharmacological effects of fenugreek are due to the presence of an alkaloid called trigonelline, which has been the subject of several studies regarding its use in the prevention and treatment of diabetes. Trigonelline has been reported to have several beneficial properties for human body which affects almost all the major aspects of human physiology. It is hypoglycemic, hypolipidemic, neuroprotective, antimigraine, sedative, memory-improving, antibacterial, antiviral, shows anti-tumor activities, and it has been shown to reduce diabetic auditory neuropathy and platelet aggregation [2].

There have been numerous studies which show the anticancer properties of fenugreek against a range of cancers. Fenugreek has several important components such as trigonelline, diosgenin and protodioscin which have been found to have anticancer properties. An important component of fenugreek, diosgenin, is a steroid saponin and has been reported to inhibit cell growth and induce apoptosis in the HT-29 human colon cancer cell line in a dose-dependent manner [3]. The mechanism of action of diosgenin was proposed to be induction of apoptosis in HT-29 cells partially by inhibition of bcl-2 and by induction of caspase-3 protein expression. This study suggested the fenugreek constituent, diosgenin, has potential as a novel preventive agent for colon cancer. A study by Jagadeesan et al. [4] showed that diosgenin exhibits anticarcinogenic activity via reducing peroxidation reaction and marker enzymes through enhancing the intrinsic antioxidant defense system. Similarly, Das et al. [5] reported antineoplastic and apoptotic potential of diosgenin in squamous cell carcinoma. Diosgenin inhibited cell proliferation and induced cytotoxicity in A431 and Hep2 cells.

Significant chemo preventive effect of fenugreek seeds against breast cancer has also been reported. Fenugreek seed extract was demonstrated to significantly inhibit MDA 231-induced mammary hyperplasia and decreased its incidence probably by induction of apoptosis [6] which may be due to its ability to increase the expression of pro-apoptotic genes [7]. One striking feature of fenugreek is its selective toxicity against cancer cells as was revealed by an interesting study which revealed fenugreek cytotoxic to a panel of cancer but not normal cells [8]. Treatment with 10–15 µg/mL of fenugreek for 72 h was found to be growth inhibitory to breast, pancreatic and prostate cancer cell lines which was due to induction of cell death as was seen by incorporation of Ethidium Bromide III into cancer cells exposed to fenugreek [8]. This may be the most promising feature of fenugreek as one of the major drawbacks of conventional chemotherapy is the toxicity and subsequent damage of normal healthy cells which leads to irreparable damage in cancer patients undergoing cancer treatment.

Another important component of fenugreek, Protodioscin (PD), has been purified from fenugreek and its effects on cell viability in Human Leukemia (HL-60) and human stomach cancer (KATO III) cells were investigated. PD displayed strong growth inhibitory effect against HL-60 cells, but weak growth inhibitory effect on KATO III cells. Morphological changes (apoptotic bodies) were observed in HL-60 cells treated with PD, but not in KATO III cells treated with PD. These findings suggest that growth inhibition of HL-60 cells by PD results from the induction of apoptosis [9]. Incubation of Jurkat T lymphocytes cells with fenugreek extract resulted in cell death in a dose- and time-dependent manner. The appearance of large vacuoles, membrane disintegration and increased expression of autophagy protein LC3 transcripts appeared as distinct morphological changes which indicated that fenugreek extract induced autophagy and autophagy associated death of Jurkat cells [10].

Methanolic and ethanolic extracts of fenugreek have also been reported to lead to tumor regression in mice and decreased viability of breast cancer cell line. Ali et al. [11] reported that methanolic extracts of fenugreek limit the rate of proliferation by inhibiting the processes leading to cancer development and also induce stable cytoplasmic expression of p53-mediated apoptosis, leading to fewer and regressed tumors in mice. Another *in vivo* study showed the antineoplastic effect of fenugreek seed extract in the Ehrlich Ascites Carcinoma (EAC) model in Balb-C mice. Intra-peritoneal administration of the alcohol extract of the seed both before and after inoculation of EAC cell in mice produced more than 70% inhibition of tumour cell growth with respect to the control. Treatment with the

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extract was found to enhance both the peritoneal exudate cell and macrophage cell counts and the extract also produced a significant antiinflammatory effect [12]. Sebastian and Thampan [13] reported that the ethanol extract of fenugreek decreased the cell viability and induced early apoptotic changes such as flipping of phosphatidylserine and decrease of mitochondrial membrane potential in breast cancer (MCF-7 cells). Moreover, the spectrum of anticancer properties of fenugreek now also includes lymphoma of nervous system with a recent study reporting anticancer properties of fenugreek in a patient with established relapsed primary Central Nervous System (CNS) lymphoma [14].

The results from these studies strongly suggest the beneficial effect of fenugreek for prevention and treatment of cancer in preclinical settings. The findings are promising and opening up new vistas in the treatment of cancer with more efficacy and lesser side effects. This could lead to a dramatic shift in the approaches of clinicians and improve the overall treatment outcomes of the cancer patients and help improve the overall well being of the cancer patients. However, the translation of the *in vitro* efficacy of fenugreek in the prevention of cancer to clinical use needs establishment of physiologically relevant concentrations and doses to sync with the *in vivo* conditions. Furthermore, there is also a need for optimizing the desired physiological response taking into consideration intake, duration, and validation in suitable animal models. Moreover, more clinical trials or further studies must also be done in order to elucidate and understand the mechanisms involved in the treatment and prevention of human cancer so as to utilize the full anticancer potential of fenugreek.

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